Surface-reaction models of protocells

Carletti, Timoteo; Serra, Roberto; Poli, Irene

Published in:
Proc. of the 2006 International Symposium on Mathematical and Computational Biology

Publication date:
2007

Document Version
Early version, also known as pre-print

SURFACE-REACTION MODELS OF PROTOCELLS

ROBERTO SERRA

Dipartimento di Scienze Sociali, Cognitive e Quantitative, Università di Modena e Reggio Emilia, via Allegri 9, 42100 Reggio Emilia, Italy

TIMOTEO CARLETTI[†]

Département de mathématique, FUNDP, 8 Rempart de la Vierge, Namur B 5000 Belgium

IRENE POLI

Dipartimento di Statistica, Università Ca' Foscari, San Giobbe - Cannaregio 873, 30121 Venezia, Italy

We present a class of models aiming to describe generic protocells hypotheses, improving a model introduced elsewhere[13]. These models, inspired by the "Los Alamos bug" hypothesis, are composed by two coupled subsystems: a self-replicating molecule-SRM- and a lipid container. The latter grows thanks to the replication of the former, which in turn can produce copies of itself thanks to the very existence of the lipid container, as it is assumed that SRMs are preferentially found in the lipid phase. Nevertheless, due to abstraction level of our models, they can be applied to a wider set of detailed protocell hypotheses. It can thus be shown that, under fairly general assumptions of generic non-linear growth law for the container and replication for the SRM, the two growth rates synchronize, so that the lipid container doubles its size when the quantity of self-replicating molecules has also doubled – thus giving rise to exponential growth of the population of protocells. Such synchronization had been postulated a priori in previous models of protocells, while it is here an emergent property. Our technique, combining a continuous-time formalism, for the growth between two successive protocell divisions, and a discrete map, relating the quantity of self-replicating molecules in successive generations, allows one to derive several properties in an analytical way.

Keywords: protocell, self-replication, dynamical model, synchronization

1. Introduction

The study of primitive cell-like structures, capable of self-replication and endowed with rudimentary metabolism and genetics, is important both for the studies about the origin of life and for possible industrial applications[8,12]. These so-called protocells have not yet been built, although several efforts are under

[†] This author will present the work at the conference if accepted.

way, hence the study of generic protocell models is particularly relevant.

Different modeling levels address different issues related to protocell behavior; here we concentrate on a class of models that allows us to study the *evolution* problem of a *populations* of *protocells*. Indeed, the evolvability of such populations is a key issue both in the origin of life problem and for application purposes, where by applying a suitable selection pressure one tries to develop populations specialized in a desirable task (e.g. drug design).

In order to be manageable, such models need to abstract from many details providing the further advantage that their conclusions can be relevant for many specific protocells that can be developed in the future.

We analyze and improve here a protocell model, previously introduced and studied in[13], loosely inspired by the so-called "Los Alamos bug" (briefly Labug in the following) hypothesis[6,7], which however abstracts from many details of Labug and can therefore be compatible also with other specific protocell models. The level of details can be compared to that of a model by Kaneko[3], who however considered the interaction of two molecular types, which catalyze each other's formation, in a way similar to that of nucleic acids and proteins. In the Labug hypothesis and also in our model, on the contrary, one deals with a single kind of Self-Replicating Molecule[§] - briefly SRM in the following - and a lipid micelle container, which in our model can be either a micelle or a vesicle. On the one hand, the presence of the SRM affects the growth rate of the container, e.g. by favoring the formation of amphiphiles from precursors, which exist in the neighborhood of the protocell outer surface (amphiphiles are supposed to be quickly incorporated in the lipid membrane). On the other hand, the very existence of the lipid container is a necessary condition for the working of the protocell, as it is assumed that SRM are preferentially found in the lipid phase.

So SRM catalytic activity favors the growth of the lipid container, which provides in turn the physical conditions appropriate for the replication of SRM, without being however a catalyst. The relationship between container and SRM is different from the one considered by Kaneko and therefore requires a different analysis. One of the main assumptions of our models is that all the reactions occur close to the surface of the protocell, that's why we called them *surface reaction models*.

In our model the SRM replication rate can be linear or sublinear, as suggested by the Labug papers[6,7] and others[5,11], coupled with the container growth, which also can be non-linear. The model is continuous in time, and the dynamics is smooth during the growth of a protocell, but it is assumed that once the membrane size reaches a critical threshold, the protocell splits into two

[§] Actually, PNA: but here we will not make any specific hypothesis about the chemical identity of the self-replicating molecules, and we will only suppose that they can be found in the lipid phase.

daughters units, as in the Chemoton model[2].

We will then consider the evolution of a population of protocells, ignoring for the time being mutations in the SRM. In particular the concentration of SRM affects the growth rate of the protocell itself, and therefore the doubling time of the population. Starting from the first protocell, which is born with a certain amount of SRM, the rate of replication of SRM will in general be different from that of the growth of the container. A consequence is that the amount of SRM at the protocell division time may be different from twice its initial value, so each daughter protocell could start with a quantity of SRM different from that of the parent protocell. Therefore the duplication time of the second generation will also be different from that of the first one. A natural question is how will these two quantities change in time, under the combined action of continuous growth and sudden division, hence the occurrence of a possible synchronization mechanism.

The synchronization phenomenon is a key ingredient to ensure a possible Darwinian evolution[1,10]. In fact if the two subsystems do synchronize then death by dilution[4] is avoided and moreover the population size grows exponentially, independently of the actual replication rate of the SRMs and/or the container, if no exogenous events arise. But exponential growth is necessary condition to have survival of the fittest in a competitive environment, hence selection among protocells.

Our main result is that, under very general assumptions, the container growth and the duplication of genetic material do synchronize in successive generations. Note that the problem of assuring consistency between the replication rates of the different protocell components is present in every Chemoton-like model, where protocell division is assumed to take place at a certain critical size. In the original Chemoton model[2] the issue is handled by assuming a priori a stoichiometric coupling between the different processes, while here *synchronization* is an *emergent property* of the model, derived without assuming ad hoc stoichiometric ratios.

In order to prove this result we introduce a mathematical technique which is well suited for this kind of problems: the continuous growth between two successive divisions allows conserved quantities, which are used to derive an iteration map for the value of the SRM quantity in successive generations. The map tends to a fixed point (thus proving synchronization) and provides quantitative information about the kinetics of protocell replication.

2. The basic model

Let us start by recalling the main model introduced in[13] which will be the starting point for the successive investigations.

Let C be the total quantity of "container", e.g. lipid membrane in vesicles or bulk of the micelle (since we assume constant density, it does not matter whether we measure C as mass or volume). Let us denote by S the surface area, which is a function of C: typically, S is approximately proportional to C for a large vesicle with a very thin surface (a condition which will be referred to as the "thin vesicle case"), and to $C^{2/3}$ for a micelle. Let X to denote the total quantity of genetic material in the protocell lipid phase.

We assume that only the fraction of the total X, which is near the external surface, is effective in catalyzing amphiphiles formation, that's because precursors are found outside the protocell. For the same reason this applies also to the replication of X itself, here the precursors are nucleotides. Let us denote volume concentrations with square brackets, therefore the total fraction of active X is proportional to $\delta S[X]_S$, where $[X]_S$ is the volume concentration of X in a layer of width δ below the external surface.

Let [P] be the concentration, in the external solution near the protocell surface, of precursors of amphiphiles: assuming it to be buffered, then it is just a constant. If the growth of the lipid membrane and the replication of SRM take both places near the surface, we have:

$$\begin{cases} \dfrac{dC}{dt} = \alpha' S[X]_S [P] + \chi S[P] - \gamma\varphi(C) \\ \dfrac{dX}{dt} = \eta' S[X]_S^{\nu} - \lambda\psi(X) \end{cases}, \qquad (2.1)$$

for some positive constants, denoted by Greek letters.

The first term of equation (2.1a) is the growth due to the transformation of precursors into amphiphiles, $P \to A$, catalyzed by the X-SRM, assuming the amphiphile A to be quickly incorporated in the membrane once produced. The second term is a spontaneous growth, due to spontaneous formation of amphiphiles, while the third term accounts for possible release of amphiphiles previously incorporated in the membrane (note that the exact form for the decay term has not been specified).

The second equation of (2.1) describes autocatalytic growth of the X-SRM (with a possible non first order kinetics described by the exponent $\nu > 0$) with degradation, because of the last term $\lambda\psi(X)$.

We now neglect the term of spontaneous amphiphile formation, which is assumed to be smaller than the catalyzed term, we assume [P]= constant, and we suppose that S is proportional to C^{β} (β ranging between 2/3 and 1). By slightly redefining the constants we obtain:

$$\begin{cases} \dfrac{dC}{dt} = \alpha'' C^{\beta} [X]_S - \gamma\varphi(C) \\ \dfrac{dX}{dt} = \eta'' C^{\beta} [X]_S^{\nu} - \lambda\psi(X) \end{cases}.$$

But $[X]_s$ is proportional to the concentration of X in the whole lipid phase, which is[**] X/C. Therefore, again incorporating constant terms in the rate constants:

$$\begin{cases} \dfrac{dC}{dt} = \alpha X C^{\beta-1} - \gamma\varphi(C) \\ \dfrac{dX}{dt} = \eta X^{\nu} C^{\beta-\nu} - \lambda\psi(X) \end{cases}. \qquad (2.2)$$

To get a feeling for the behavior of equations (2.2), let us consider the growth of a vesicle container with a very thin membrane ($\beta \cong 1$) in the case where X is constant and $\varphi(C)=C$. Then the first equation rewrites:

$$\frac{dC}{dt} = k - \gamma C ,$$

where $k = \eta X_0$ is a constant, X_0 being the initial concentration of SRM. This equation can be explicitly solved and thus we can describe the growth of the lipid container up to its asymptotic value k/γ (provided that the initial value C_0 is smaller than k/γ).

We will assume that the protocell breaks into two identical daughters units when its size reaches a certain threshold θ. Moreover, we will assume that the growth is essentially exponential, i.e. that the rate limiting steps in Eq. (2.2) above do not play a significant role when $C < \theta$. Therefore the growth of a protocell up to its critical size is approximately ruled by the following equations (coming back to a generic container and non constant X):

$$\begin{cases} \dfrac{dC}{dt} = \alpha X C^{\beta-1} \\ \dfrac{dX}{dt} = \eta X^{\nu} C^{\beta-\nu} \end{cases}. \qquad (2.3)$$

This system of equations (2.3) will be the starting point for our further

[§] We assume here that transport in the lipid phase is extremely fast, leading to homogeneous concentrations of SRM in the whole vesicle membrane or micelle.

analysis in the next sections.

Let just observe that in the case two different, non-interacting SRMs were present in the same protocell, the model (2.3) can be generalized into:

$$\begin{cases} \dfrac{dC}{dt} = \alpha' C^{\beta-1} X + \alpha'' C^{\beta-1} Y \\ \dfrac{dX}{dt} = \eta' C^{\beta-\nu} X^{\nu} \\ \dfrac{dY}{dt} = \eta'' C^{\beta-\nu} Y^{\nu} \end{cases}, \tag{2.4}$$

assuming the general growth rate of the container depending on both the SRMs.

These two models, (2.3) and (2.4) have been introduced in[13] and extensively analyzed there, we thus invite an interested reader to refer to them for further details. Nevertheless, for the sake of completeness, we will report in the next paragraph some relevant results obtained in[13].

2.1. *Summary of some known facts concerning the basic model*

One main feature of our model is that is it able to provide a unified treatment of both micelle and vesicle cases. More precisely it has been proved that, up to an appropriate non-linear rescaling of time, the behavior of the micelle model and the thin vesicle case are asymptotically qualitatively the same. Thus all our computations we will be explicitly ruled out in the thin vesicle case, $\beta=1$, because computationally simpler.

Let us sketch this proof here for sake of completeness. Indeed let us observe that C(t) is positive for any finite t, so one can define a new time by:

$$\tau = \tau_0 + \int_0^t C(s)^{\beta-1} ds ,$$

note that $d\tau/dt=C(t)^{\beta-1}$. Let now $\omega(t)$ be a quantity which satisfies a differential equation of the form

$$\frac{d\omega(t)}{dt} = C(t)^{\beta-1} F(\omega(t)),$$

for an arbitrary function F. Define $\psi(\tau)\equiv\omega(t(\tau))$, i.e. the same quantity ω but read in the new time variable, then its evolution is given by:

$$\frac{d\psi(\tau)}{d\tau} = \frac{dt}{d\tau}\frac{d\omega(t)}{dt} = F(\psi(\tau)).$$

Let us now apply this idea to equation (2.3) by defining $c(\tau)=C(t(\tau))$, $x(\tau)=X(t(\tau))$: in terms of the new variables, using the previous remarks, these equations become:

$$\begin{cases} \frac{dc}{d\tau} = \alpha x \\ \frac{dx}{d\tau} = \eta x \end{cases},$$

which can be considered as the equations describing the container growth and SRM replication in a vesicle protocell.

To summarize the known results let us consider separately the case where the growth of the self-replicating molecules is linear, from the one where it is sublinear. In the former case it has been proved that:

i) When only one kind of SRM is present, then the doubling time depends only upon the rate constant for self-replication (so if there are two kinds of protocells, one with higher α and lower η than the other, the former will eventually be outperformed by the latter);

ii) If there are two different SRMs in the same protocell, the one, which is slower in replicating itself, vanishes in the long time limit, even if it can provide a faster growth rate for the container (and in the case of fast parasites these will dominate and lead to halting the growth).

In the case where the growth of the self-replicating molecules is sublinear, it has been shown that:

iii) The synchronization still occurs in the case of only one kind of SRM;

iv) When two different SRMs exist in the same protocell, the ultimate fate of the system is coexistence of both SRMs, reaching fixed ratios.

3. Non-linear growths for the container

The main hypothesis used to derive the model (2.3) is that the container growth is linear in the concentration of X-SRM. This can be considered true in first approximation if the involved concentrations are small; on the other hand some non-linear phenomena can occur when concentrations increase. The main goal of this section is to prove that our analysis can be extended as to consider generic

growth rates for the container, in particular also an auto inhibitory effect can be taken into account: large concentration of SRM can stop the container growth.

Let the container growth be described by some *positive* function ψ(s) of a real positive variable s, and assume the following:

a) ψ(0)=0, namely the container doesn't grow if there are no SRM at all;
b) There exists a positive constant L, such that for all s > 0, we have: ψ(s) ≤ L, namely the instantaneous growth rate of the container is always finite.

Assuming a linear reproduction law for the SRM, model (2.3) can thus be generalized into:

$$\begin{cases} \dfrac{dC}{dt} = C^{\beta}\psi\left(\dfrac{X}{C}\right) \\ \dfrac{dX}{dt} = \eta X C^{\beta-1} \end{cases}. \tag{3.1}$$

The main result of this section is that synchronization is a emergent property of our model once non-linear growth for the lipid container is take into account, as stated by the following

Theorem

Let us denote by X_k the initial amount of X-SRM, inside the container, at the k^{th} division and let $\eta > 0$ and $2/3 \le \beta \le 1$ be assigned positive constants. Then under the previous assumptions of the function ψ, we have the following mutually exclusive results:

(1) If $\eta > \psi(\xi)$ for all ξ then $X_k \to \infty$ when k increases.
(2) There exist $N \ge 1$ positive values ξ_i such that $\psi(\xi_i) = \eta$, assume moreover such roots to be transversal[††] and ordered in increasing magnitude, $\xi_1 < \ldots < \xi_i < \ldots \xi_N$. Then there are $N' = \lfloor (N+1)/2 \rfloor$ possible asymptotic values for X_k: $\Xi_{2l-1} = \theta\xi_{2l-1}/2$ for $l=1,\ldots,N'$. More precisely the actual value is fixed by the initial condition: if X_0 belongs to (Ξ_{2l-2},Ξ_{2l}), for some $l=1,\ldots,N'$, then $X_k \to \Xi_{2l-1}$.

The proof of this result will be given in the next paragraph.

3.1. *Synchronization for generic non-linear growth of lipid containers.*

To analyze model (3.1) let us introduce an auxiliary variable ξ(t)=X(t)/C(t),

[††] This means that the function η−ψ(ξ) changes signs at ξ = ξ_i.

which allows to rewrite it as follows:

$$\begin{cases} \dfrac{dC}{dt} = C^{\beta}\psi(\xi) \\ \dfrac{d\xi}{dt} = C^{\beta-1}\xi(\eta - \psi(\xi)) \end{cases}. \tag{3.2}$$

Let us distinguish to cases, according to η is larger than $\psi(\xi)$ for all ξ or there exists at least one positive values ξ_1 such that $\psi(\xi_1) = \eta$.

In the first case, equation (3.2b) implies that $\xi(t)$ is an increasing function, except the trivial case: $\xi(0) = 0$, which means complete absence of SRM at the beginning, and thus it can be discarded. Hence for all positive t, we have $\xi(t) > \xi(0)$. On the other hand equation (3.2a) implies that also C(t) is an increasing function, and thus starting from $C(0) = \theta/2$, there always exists a positive time T, such that $C(T)= \theta$. An estimate for T can be obtained using assumption b) on ψ, in fact (3.2a) gives:

$$\frac{dC}{dt} = C^{\beta}\psi(\xi) \le LC^{\beta}$$

thus by simple integration we obtain:

$$\begin{cases} \beta < 1 \Rightarrow T \ge \dfrac{\theta^{1-\beta}}{L(1-\beta)}\left(1 - \dfrac{1}{2^{1-\beta}}\right) \\ \beta = 1 \Rightarrow T \ge \dfrac{1}{L}\log 2 \end{cases}.$$

Back in the original variables, X and C, we get:

$$X(0) = C(0)\xi(0) = \frac{\theta}{2}\xi(0) \text{ and } X(T) = C(T)\xi(T) = \theta\xi(T)$$

and recalling the halving hypothesis at the division: each offspring will start with an initial concentration of SRM equal to $X_1=X(T)/2$, we thus obtain:

$$X_0 = \frac{\theta}{2}\xi(0) \text{ and } X_1 = \frac{\theta}{2}\xi(T).$$

Hence we can conclude that if $\eta > \psi(\xi)$ for all ξ, then for any initial concentration of SRM X_0 the successive generation will start with a larger amount of SRM:

$$X_1 = \frac{\theta}{2}\xi(T) > \frac{\theta}{2}\xi(0) = X_0 .$$

This of course holds true for any division and thus we conclude that in this case the number of SRM grows unbounded.

Still using the new auxiliary variables, ξ and C, let us now consider the remaining case: there exist N positive values ξ_i such that $\psi(\xi_i) = \eta$. This means that the function $f(\xi) = \xi(\eta - \psi(\xi))$ has N+1 roots, the N ones of ψ and $\xi_0=0$. Each root of f corresponds to a steady solution of (3.2b) while discarding the division mechanism. By assumption each root is transversal and they are ordered by increasing magnitude, thus performing a local stability analysis in neighborhoods of each root, we can prove that *even indexed* roots are *unstable equilibria*, while *odd indexed* are *stable*[##].

A simple analysis of the one-dimensional system, still discarding the division mechanism, tell us that for any $\xi(0)$ in $I_{2l}=(\xi_{2l-2}, \xi_{2l})$, for some l=1,…,N', then $\xi(t)$ will asymptotically converge to ξ_{2l-1}, observe the minus sign in front of $\psi(\xi)$ which reverses the usual stability condition related to the sign of the first derivative. Moreover $\xi(t)-\xi_{2l-1}$ has the same sign than $\xi(0)-\xi_{2l-1}$ and $|\xi(t)-\xi_{2l-1}|<|\xi(0)-\xi_{2l-1}|$, namely the orbit never leaves the interval I_{2l}.

Let us now introduce the division mechanism and go back to the original variables. The equation (3.2a) still implies again that C(t) is an increasing function of time and thus there always exists a division time T, $C(T)=\theta$ if $C(0)=\theta/2$. To each roots ξ_l we associate the values $\Xi_l = \theta\xi_l/2$ and the intervals $J_{2l}= (\Xi_{2l-1}, \Xi_{2l+1})$.

The behavior in the ξ variables can be translated for the X variables, as follows. For X_0 belonging to some J_{2l}, then, calling T the division time, we have:

$$X_0 = C(0)\xi(0) = \frac{\theta}{2}\xi(0) \quad \text{and} \quad X_1 = \frac{X(T)}{2} = \frac{C(T)\xi(T)}{2} = \frac{\theta}{2}\xi(T),$$

moreover:

$$\left|X_1 - \Xi_{2l}\right| = \left|\frac{\theta}{2}\xi(T) - \frac{\theta}{2}\xi_{2l}\right| < \left|\frac{\theta}{2}\xi(0) - \frac{\theta}{2}\xi_{2l}\right| = \left|X_0 - \Xi_{2l}\right|$$

and $X_1 - \Xi_{2l}$ has the same sign that $X_0 - \Xi_{2l}$. Namely X_1 still belongs to J_{2l} and it is closer to Ξ_{2l} than X_0. The same considerations hold for the second generation, which start with an initial amount of X-SRM of X_1; we can thus construct in this way a sequence of initial amount of X-SRM at each generation

[##] Setting $u = \xi - \xi_i$ we get from (3.2b): $\dot{u} = -C^{\beta-1}(u+\xi_i)\psi'(\xi_i)u + \ldots$, and the stability claim is thus obtained.

X_k, converging to Ξ_{2l}. Once X_k converges to a fixed value, the same holds true for the division time and thus synchronization is obtained as *emergent property* of the model, moreover the asymptotic value for the amount of X-SRM depends on η but also on the growth rate of the container.

Let us observe that the transversality assumption, even if it is generically verified - if for some value of η we have a non-transversal root, just by slightly changing η the root is preserved and it becomes a transversal one - can be relaxed without changing the analysis of the model, except the rate at which now the synchronization is reached, which will be slower in this case.

4. Non-linear replication rate for the SRM

In this section we relax the second hypothesis of the basic model (2.3) by allowing general non-linear rates for the replication of SRM. The linear (or the sublinear) rates analyzed in[13] representing particular cases, while the analysis described here is definitely more general and largely independent from specific hypotheses.

Let the replication rate be described by some positive function $\phi(s)$ of a real positive variable s, and assume the following:

c) $\phi(0)=0$, namely the SRM doesn't replicate if there are no SRM at all. More precisely there exists $0 < p < 2$ such that for s sufficiently small we have $\phi(s) \sim s^p$.

d) There exists a positive constant M, such that for all $s > 0$, we have: $\phi(s) \leq M$, namely the instantaneous replication rate of SRM is always finite.

Observe that if we introduce the hypothesis that $\phi(s)$ goes to 0 when s becomes unbounded, this model can describe an auto inhibitory mechanism for the template replication: too many SRMs prevent the container growth.

Assuming a linear container growth with respect to the amount of X and the previous assumptions on the replication rate of SRMs, then model (2.3) can be rewritten as follows:

$$\begin{cases} \dfrac{dC}{dt} = \alpha C^{\beta-1} X \\ \dfrac{dX}{dt} = C^{\beta} \phi\left(\dfrac{X}{C}\right) \end{cases}. \tag{4.1}$$

The main result of this section is that synchronization is a emergent property of our model once self-replication has a generic non-linear, as stated by the following theorem which will be proved in the next paragraph.

Theorem

Let us denote by X_k the initial amount of X-SRM, inside the container, at the k^{th} division and let $\alpha > 0$, $\eta > 0$ and $2/3 \leq \beta \leq 1$ be assigned positive constants. Under the previous assumptions of the function ϕ, let us call Λ the set of roots of the equation $g(\zeta) = \phi(\zeta) - \alpha\zeta^2$ *and assume they are all transversal. Then* $X_k \to \theta\zeta_i/2$ *where ζ_i is an element of Λ such that $\phi'(\zeta_i) - 2\alpha\zeta_i < 0$; toward which element actually X_k does converge depend on the initial concentration X_0.*

4.1. *Synchronization for generic non-linear growth of self-replicating molecules.*

Once again to analyze this model let us introduce an auxiliary variable $\zeta(t)=X(t)/C(t)$, which allows to rewrite (4.1) as follows:

$$\begin{cases} \dfrac{dC}{dt} = \alpha C^{\beta}\zeta \\ \dfrac{d\zeta}{dt} = C^{\beta-1}\left(\phi(\zeta) - \alpha\zeta^2\right) \end{cases}. \tag{4.2}$$

Let us analyze this model by starting with the trivial fixed point $\zeta = 0$. Assumption c) implies that if ζ is sufficiently small, but positive, then $\phi(\zeta)-\alpha\zeta^2 \sim \zeta^p$, hence positive, namely the origin is an unstable equilibrium point.

Assumptions c) and d) imply that the functions $\phi(\zeta)$ and $\alpha\zeta^2$ have at least a non-zero intersection point; moreover all the intersection points are contained in the bounded interval $[0,\Delta]$, where $\Delta = \sqrt{M/\alpha}$. We can also assume these intersection points to be transversal ones.

Let us call ζ_i the Q distinct (Q = 1 is allowed) positive intersections points of the functions $\phi(\zeta)$ and $\alpha\zeta^2$, namely the roots of the function $g(\zeta) = \phi(\zeta) - \alpha\zeta^2$. Once again let us divide these points into two groups: a first group denoted by $\Lambda^<$ is formed by those for which $\phi'(\zeta_i) - 2\alpha\zeta_i < 0$, and a second group, denoted by $\Lambda^>$ for which $\phi'(\zeta_i) - 2\alpha\zeta_i > 0$ together with $\zeta = 0$. Moreover to each ζ_i in $\Lambda^<$ we can uniquely associate two elements $\zeta_1^> < \zeta_i < \zeta_2^>$ in $\Lambda^>$ and an interval[§§] $I_i = \left(\zeta_1^>, \zeta_2^>\right)$.

Discarding for the time being the division mechanism, a simple analysis of the one-dimensional system (4.2b), tell us that for any $\zeta(0)$ in I_i, then $\zeta(t)$ will converge to ζ_i as t increases. Moreover $\zeta(t)-\zeta_i$ has the same sign than $\zeta(0)-\zeta_i$ and $|\zeta(t)-\zeta_i|<|\zeta(0)-\zeta_i|$, namely the orbit never leaves the interval I_i.

Let us now consider the division mechanism and go back to the original variables. The equation (4.2a) implies again that C(t) is an increasing function of

[§§] In the case there exists only one root, we set $I_i=(0,\infty)$.

time and thus there always exists a division time T, C(T)=θ if C(0)=θ/2. To each root ζ_i we can associate a value $Z_i=\theta\zeta_i/2$, hence an interval $J_i = \left(Z_1^>, Z_2^>\right)$, where for l=1,2: $Z_l^> = \theta\zeta_l^> /2$, and $\zeta_l^>$ have been defined previously.

The behavior of the ζ variables can be straightforwardly translated into the following one for the X variables. For X_0 belonging to some J_i then, calling T the division time, we have:

$$X_0 = C(0)\zeta(0) = \frac{\theta}{2}\zeta(0) \quad \text{and} \quad X_1 = \frac{X(T)}{2} = \frac{C(T)\zeta(T)}{2} = \frac{\theta}{2}\zeta(T),$$

moreover:

$$\left|X_1 - Z_i\right| = \left|\frac{\theta}{2}\zeta(T) - \frac{\theta}{2}\zeta_i\right| < \left|\frac{\theta}{2}\zeta(0) - \frac{\theta}{2}\zeta_i\right| = \left|X_0 - Z_i\right|$$

and $X_1 - Z_i$ has the same sign of $X_0 - Z_i$. Namely X_1 still belongs to J_i and it is closer to Z_i than X_0. Thus can repeat the same consideration for the second generation which start with an initial amount of X-SRM of X_1, thus we construct in this way a sequence of initial amount of X-SRM at each generation X_k, converging to Z_i.

Hence we can conclude that synchronization is achieved and it is an emergent property of the model; moreover the asymptotic value for the amount of X-SRM depends, of course, on the function ϕ, but also on α, namely the "speed" of growth rate of the container.

Let us observe that the transversality assumption can be relaxed without changing the analysis of the model, the only change is in the rate at which now the synchronization is reached, which will be slower in this second case.

A "simple" function which verify our assumptions is

$$\phi(s) = \frac{s^p}{a^2 + b^2 s^{p+q}},$$

for some positive p < 2 and q > 0.

5. Conclusions

In this paper we have improved a basic model introduced in[13] to describe a class of abstract protocells hypotheses, called *surface reaction model* because the mechanisms responsible for the growth of the lipid container and the self-replicating molecules are assumed to take place near the cell surface. Although the inspiration was drawn from the Los Alamos bug hypothesis, the high abstraction level of our models may allow their application to a broader set of

detailed models.

We also introduced a powerful analytical technique to study the behavior of this class of protocell models, which combines continuum methods, used to describe the growth between two successive protocell duplications, and discrete maps which relate the initial value of the relevant quantities of two successive generations. This technique also allows us to draw conclusions on the asymptotic properties of a micelle or a thin vesicle, by analyzing the "thin vesicle" case only, i.e. $\beta=1$.

It has been shown that, under general non-linear growth for the container or the replication rate of SRM, the replication rate becomes constant in the long time limit, which in turn implies exponential growth of the population of protocells, unless there are other limitations to growth. Synchronization of container and SRM duplication is here an emergent property, while in earlier models, like the Chemoton, it was imposed a priori through a stoichiometric coupling. This phenomenon of exponential growth for the population size, could eventually produce a Darwinian selection in the group.

We recently became aware of the fact that a similar synchronization has been demonstrated by Rasmussen and co-workers in another protocell model, using a different approach[9] assuming linear growth for the container and a sublinear one for the SRM replication. This suggests that such synchronization phenomena may be "generic", i.e. common to several protocell models

In the case where the growth of the self-replicating molecules is fully non-linear, it has been shown here that several possible asymptotic values for the amount of SRM in the protocell, can be present, the one which will be chosen depend on the initial amount of SRM and on a peculiar relation between the function describing the growth rate of the SRM and the "speed" of the container growth. A similar result is obtained when considering a non-linear growth for the container.

The models we studied are quite general and they can be applied to describe several specific systems.

Acknowledgments

This work was funded by PACE (Programmable Artificial Cell Evolution), a European Integrated Project in the EU FP6-IST-FET Complex Systems Initiative. We also thank the participants to the PACE workshop on "Evolution and Self-assembly" held at the European Center for Living Technology on march 16-19, 2006, with which we had stimulating and useful discussions, in particular John McCaskill, Norman Packard, Steen Rasmussen and Marco Villani for their helpful comments. We also gratefully acknowledge the help of Michele Forlin in the preparation of this paper.

References

1. M. Eigen and P. Schuster, Naturwiss., **64**, 541, (1977).
2. T. Gánti, New York, Kluwer Academic/Plenum Publishers, (2003).
3. K. Kaneko, Advances in Chemical Physics **130B**, 543, (2005).
4. P.L. Luisi, F. Ferri and P. Stano, Naturwiss., **93**, 1, (2006).
5. A. Munteanu, C.S. Attolini, S. Rasmussen, H. Ziock, and R.V. Solé, submitted, (2006).
6. S. Rasmussen, L. Chen, M. Nilsson and S. Abe, Artificial Life **9,** 269, (2003).
7. S. Rasmussen, L. Chen, B. Stadler and P. Stadler, Origins Life & Evol. Biosph. **34,** 171, (2004).
8. S. Rasmussen et al, Science **303**, 963-965, (2004).
9. T. Rochelau et al, submitted, (2006).
10. E. Szathmáry and J. Maynard Smith, J. Theor. Biol., **187**, 555, (1997).
11. B. Stadler and P. Stadler, Adv. Comp. Syst. **6,** 47, (2003).
12. D. Szostak, P.B. Bartel, and P.L. Luisi, Nature **409**, 387, (2001).
13. R. Serra, T. Carletti and I. Poli, in press Artificial Life, (2006).